REMARKS

Claims 2 and 23 are pending at the present time. The Office has indicated that claim 2 is allowed.

Claim 23 is rejected under 35 U.S.C. §103(a) as unpatentable over Diamond et al., U.S. Patent No. 6,156,317, in view of Gallina et al. The Office states that Diamond et al. "clearly teach a mutant cytomegalovirus protein (pp65) which elicits a CTL response against cells infected with cytomegalovirus," but is silent with respect to protein kinase activity of pp65 or the variants. See Office Action, page 2.

A clear reading of Diamond et al. reveals that this patent does not disclose, discuss, mention, or even hint at a mutant pp65 protein. The word "mutant" does not occur in the patent specification. The Diamond et al. reference relates to immunologically functional variant epitope peptides which are not mutant forms of viral protein, but rather small peptides based on a wild type sequence and synthesized chemically, with variations according to binding motifs. No mutant protein is used or even mentioned in the methods of Diamond et al. A sequence from non-mutant, wild type pp65 was discovered to be an immunologically active epitope of pp65. With this knowledge, the inventors synthesized short peptides based on the native sequence, and prepared different variant peptides which had sequences based on the native sequence by chemical synthesis. No protein was mutated. Therefore the Diamond et al. patent lacks any teaching whatsoever regarding mutant pp65 proteins.

The Office has conceded, as it must, that the reference is silent as to pp65 protein kinase activity. Neither the wild type protein nor any of the CTL epitope peptides based on sequences from the wild type protein were examined for protein kinase. It is not likely that any of the short, variant peptide epitopes of

Diamond et al. could possess enzymatic activity since they all are less than 12 amino acids in length, however these variants are neither mutants nor proteins. The native pp65 protein was not examined for activity. The reference is completely silent with respect to kinase activity. Therefore, there is no hint or even the slightest motivation such that a skilled artisan reading this disclosure would be aware of kinase activity or develop any motivation to test for or eliminate such activity. The Diamond et al. reference relates to short peptide epitopes, not proteins or enzymes and would not show the reader how to attain this even if motivation were present.

Therefore, the Diamond et al reference lacks any teaching or suggestion of a mutant pp65 that lacks protein kinase activity and that elicits a CTL response against cells infected with cytomegalovirus.

The Gallina et al. reference does not make up for the deficiencies of Diamond et al. This reference is cited only for the teaching that "experiments are inconclusive with respect to pp65 possessing protein kinase activity" and that "whether or not all isolated pp65 is inherently lacking in protein kinase is unclear." See Office Action, page 2. However, the Office concludes from this self-described inconclusive and unclear teaching that mutant pp65 inherently lacks protein kinases activity. This conclusion is not warranted from the cited reference. The Gallina et al. reference provides no evidence whatsoever to support the concept that pp65, alone, does not have kinase activity. Further, the authors cite many papers that support the concept that pp65 is linked to kinase activity. See, e.g., p. 1475 col. 2. The terminology used in Gallina et al. indicates that any conclusion on their part regarding the likelihood that pp65 lacks kinase activity is speculative. See, e.g., p. 1476, col. 2 ("[t]he functional significance of pp65-

Plk1 interaction can be at present only matter for speculation").

Furthermore, subsequent to the Gallina et al. paper there has been no substantiation of this hypothesis by these investigators or by others. On the other hand, the hypothesis that pp65 has no intrinsic kinase activity is disproven by Yao et al. (*Vaccine* (19:13-14):1628-1635, 2001), which already is of record in this application (see Information Disclosure Statement filed December 11, 2002). This paper clearly demonstrates that bacterially-expressed and immunoprecipitated wild type pp65 has kinase activity that is absent after mutating the phosphate binding site of the protein. Thus the speculations of Gallina et al., relied on here by the Office, are not substantiated in the cited reference itself and have been disproven by later work. The skilled person therefore would not consider Gallina et al., or the art generally, to fairly suggest to the art that pp65 inherently lacks kinase activity.

The combination of these two cited references therefore does not render the present application obvious. The references, even if their teaching were to be combined by a skilled artisan, lack at least one element of the claimed invention. There is no fair teaching or suggestion in the art of a mutant pp65 protein or of such a pp65 protein that lacks kinase activity. There is no motivation to combine the teachings of the two cited references because Diamond et al. teach methods to design peptide epitopes and Gallina et al. relates to kinase activity - Diamond et al. does not even hint that kinase activity may be important in vaccine production, so there is no reason for a skilled artisan even to be concerned about this issue or to connect these two references in any way. There is no reason for the skilled artisan to expect mutating pp65 to remove kinase activity would lead to a useful vaccine. Therefore, the Office cannot meet even

one of the criteria necessary to make out a prima facie case of obviousness against the presently rejected claim.

Applicant respectfully submits that claim 23 is novel and nonobvious with respect to the cited references and requests, for the reasons discussed above, that the Office withdraw the rejection of this claim under 35 U.S.C. §103(a).

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